

Lipton RB, Goebel H, et al. *Petasites hybridus* root (butterbur) is an effective preventive treatment for migraine. Neurology 2004;63:2240-2244.

Design: Randomized clinical trial

Population/sample size/setting:

- 202 patients with episodic migraine (166 women, 36 men, mean age 42) enrolled in a multicenter trial in Berlin, New York, and Baltimore
- Eligible patients were 18 to 65 meeting International Headache Society criteria for migraine, with 2 to 6 attacks per month in the 3 months before treatment
 - o A 4-week baseline period of observation was required, during which at least 2 migraine attacks were required in order to continue to randomization
- Exclusion criteria were non-migraine headache for 6 days per month or more; women who were pregnant or were at risk of pregnancy were excluded

Main outcome measures:

- Randomized to one of three groups: placebo twice daily, 50 mg *Petasites* extract twice daily, and 75 mg *Petasites* extract twice daily
- Identical capsules were extracted and prepared according to specifications of the German Health Authority to eliminate detectable levels of potentially hepatotoxic plant alkaloids
- Following the 4 week period of baseline observation, treatment with *Petasites* or placebo was continued for 4 months
- Main endpoint was the reduction in frequency of migraine attacks per month relative to baseline
 - o Intention-to-treat analysis showed an average migraine frequency reduction of 45% in the 75mg *Petasites* group, 32% in the 50 mg *Petasites* group, and 28% in the placebo group
 - *Petasites* 75 mg was judged more effective than *Petasites* 50 mg or placebo; *Petasites* 50 mg was judged no more effective than placebo
- Outcomes were also reported in terms of patient response, in which a “responder” had a 50% reduction in mean attack frequency per month
 - o At 4 months, the 75 mg *Petasites* group recorded 68% responders, compared to 56% in the *Petasites* 50 mg group and 49% in the placebo group; again, the 50 mg dose was not judged different from placebo, but the 75 mg dose was judged superior to both alternatives
- Adverse effects were similar between groups; differences in frequency were reported only for burping being more common with *Petasites* treatment
- There were no changes from baseline in liver transaminases, GGT, or bilirubin; blood pressure and heart rate were unaffected by treatment

Authors' conclusions:

- 75 mg of *Petasites* extract is an effective intervention for reducing the frequency of migraine attacks in patients with episodic migraine
- The placebo response rate was high, perhaps due to the medically naïve study population, all of whom may have had benefits from education about trigger avoidance and self-management of migraine
- Patients must be cautioned against consuming any part of the *Petasites* plant in any form other than the commercial extract, from which plant carcinogens have been removed

Comments:

- Allocation concealment is not quite clear; other important threats to bias appear to have been adequately controlled
- There is scant information concerning previous migraine treatment; the study population is identified as medically naïve, implying that the patients had not previously received numerous standard treatments without effect
 - o Since details of patient recruitment are sparse, the population is difficult to characterize, but they were willing to try an herbal therapy for migraine and may have had an interest in this approach
- In Figures 3 and 4, the therapeutic response to 75 mg *Petasites* appears to be slightly greater at the measurement for Month 3 than for Month 4, but the decrease in treatment effect from Month 3 to Month 4 appears to be small

Assessment: Adequate for evidence that *Petasites* extract may be effective for prophylaxis of episodic migraine